The Biospecimen Research Network of the National Cancer Institute

Scientific Retreat

March 28, 2006

Carolyn Compton, MD, PhD

Director of the Office of Biorepositories and Biospecimen Research

Compelling Factors that Make Biorepositories and Biospecimens a High Priority for the NCI

NCI Investments in the Future:
The Pathway to Personalized Medicine

- Largest contingent of investigators ever assembled to conquer a disease
- CaBIG infrastructure for “connectivity”, large-scale databases, and inter-institutional studies
- Proteomics programs for biomarker discovery and technology and standards development
- NCI-NHGRI program to characterize the “cancer genome”
- Nanotechnology initiative to develop advanced systems for cell interaction for diagnosis and treatment

NCI and the Pathway to Personalized Medicine

These and many other initiatives required to conquer cancer and realize a future of personalized molecular medicine have one common need:

HUMAN BIOSPECIMENS

High-Quality Biospecimens: The Key to the Future of Molecular Medicine

- Biorepositories with high-quality biospecimens and data are needed to:
  - Support development of genomic, proteomic analysis
  - Identify targets for therapy, detection, and prevention
  - Develop a molecular-based taxonomy of cancer
  - Ultimately realize the era of personalized medicine

The NCI Focuses on Human Biospecimens

- 2002: critical importance of biorepositories identified by NCI leadership
- Unprecedented internal and external review process
  - 2002: Initial NCI surveys, community forums
  - 2003: RAND Report and NBN Blueprint published;
    Prostate cancer NBN pilot planning initiated
  - 2004: NCI internal study of biorepositories - meetings with NCI staff who oversee biorepositories;
    Prostate cancer NBN pilot plan finalized

Process Continues 2005

- NCI Biorepository Coordinating Committee (BCC) formed
- NCI Board of Scientific Advisors Tissue Subcommittee formed
- National Biospecimen Network Prostate SPORE Pilot launched
- Dr. Compton joins NCI
- Office of Biorepositories and Biospecimen Research (OBBR) established
- Extensive review of existing Best Practices for biorepositories from authoritative sources: NCI whitepapers issued
- Two national workshops held to review the state of the science
- 1st Generation NCI Guidelines for biorepositories issued

The Path Ahead: 2006

- Historic event: Biospecimen Research Network forms
- Biospecimen Research: Scientific investigation of environmental and clinical variables that change the quantity and quality of biomolecules in human specimens
- Future generations of NCI guidelines:
  - Evidence-based SOPs for human biospecimens
  - Data-driven quality indicators for biorepositories and legacy specimen collections
  - Future standards of care for personalized molecular medicine

NCI-Supported Biospecimen Resources: Rand Investigates

- Number of NCI programs that collect human biospecimens
- Number of cancer/normal cases & specimens collected
- Specimen preservation methods
- Databases and automated specimen tracking
- Patterns of sample distribution
- SOPs, informed consent, QA/QC measures used
- Level of NCI funding

Rand Inventory Results

- Widespread heterogeneity in practices among NCI-supported programs identified
  - **Lack** of common biorepository SOPs, standards, and management principles
  - **Lack** of common definitions
  - **Lack** of computerized, common access to information on specimens and cases
  - **Lack** of access to information on available specimens
  - **Lack** of systematic coordination and distribution

NCI's Biospecimen Issues

- Despite an NCI investment in biorepositories of $50 million/yr, researchers still don't have what they need
  - #1 obstacle to progress in cancer research
- National-level biorepository standards are lacking
- NCI can't accurately evaluate what it has
- NCI can't regulate quality of specimens
- NCI can't rely on quality of resultant data

The Quality Concept: Key Requirements for a National Biospecimen Network (NBN)

- All cancer types represented
- Access through a timely, centralized peer-review process
- Ethical and privacy compliance through a chain of trust
- Resources provided without IP restrictions
- Pathology and clinical annotation (including longitudinal)
- State-of-the-art IT system
- Communication and outreach efforts
- **Best practice- and data-driven based SOPs to enable reproducible and comparable (additive) results**

The NBN Pilot: The Prostate SPOREs

- Concept
  - A biomarkers study designed to pilot key aspects of an NBN-like concept within the 11 Prostate Cancer SPOREs

Needle Biopsy Processing Protocols – 7 SPORE Sites

		Harvard		U Wash		Hopkins		U. Michagan		MD Anderson		Mayo Clinic		MSKCC	
	Condition	Time	Temp	Time	Temp	Time	Temp	Time	Temp	Time	Temp	Time	Temp	Time	Temp
Post-Fixation	10% Formalin	-	-	-	-	2	40	20	37	-	-	20	?	30	40
	10% Formalin	-	-	-	-	2	40	20	37	30	RT	-	-	30	40
	Penfix	-	-	10	37	-	-	-	-	-	-	-	-	-	-
	10% formalin in 95% eto	-	-	-	-	-	-	-	-	30	RT	-	-	-	-
Dehydration	70% ethanol	5	RT	-	-	2	40	20	37	30	RT	-	-	20	40
	70% ethanol	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	80% ethanol	15	RT	-	-	-	-	20	37	-	-	2	?	-	-
	80% ethanol	15	RT	-	-	-	-	-	-	-	-	5	?	-	-
	95% ethanol	15	RT	10	37	2	40	30	37	30	RT	-	-	10	40
	95% ethanol	15	RT	10	37	2	40	30	37	-	-	5	?	20	40
	100% ethanol	15	RT	10	37	2	40	35	37	30	RT	5	?	10	40
	100% ethanol	15	RT	10	37	-	-	35	37	30	RT	15	?	10	40
	100% ethanol	-	-	-	-	-	-	-	-	30	RT	-	-	20	40
	100% etoh/ 17%eosin	-	-	-	-	2	40	-	-	-	-	-	-	-	-
	50% etohl/ 50% Xylene	-	-	-	-	5	40	-	-	-	-	-	-	-	-
Clearing	Xylene	15	RT	10	37	2	40	35	37	30	RT	5	?	15	40
	Xylene	15	RT	10	37	2	40	40	37	30	RT	5	?	15	40
	Xylene	20	RT	10	37	-	-	-	-	-	-	-	-	-	-
Infiltration	Paraffin	20	RT	10	58	2	60	15	60	30	60	30	?	15	60
	Paraffin	20	RT	10	58	2	60	25	60	30	60	2	?	15	60
	Paraffin	-	-	10	58	5	60	25	60	30	60	-	-	20	60
	Paraffin	-	-	-	-	5	60	15	60	-	-	-	-	-	-
Total Time (minutes)		185		110		37		365		360		94		230	

Biorepository Coordinating Committee (BCC)

- Membership: Representatives from NCI divisions
- Mission: To provide leadership for biobanking activities that support all research funded by the NCI
- Process: Address harmonization of policies for biorepositories across the NCI
- Initial approach: Exhaustive review of the literature from authoritative sources and extensive input from the scientific community (state of the science workshops)

NCI-BCC Sponsored Workshops

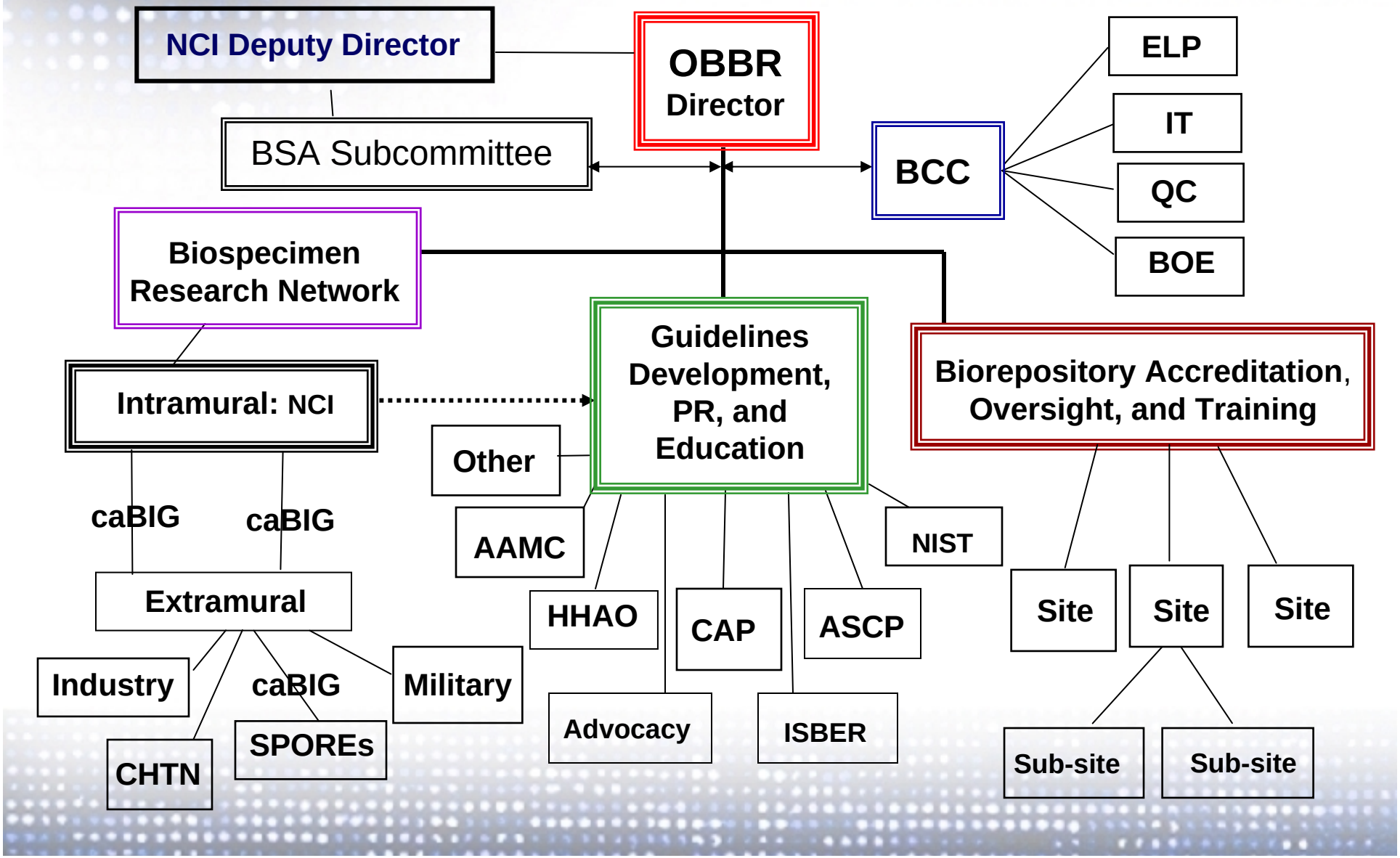
- State of the Science Workshops
  - Best Practices for Establishing and Maintaining Biorepositories that Support Cancer Research
    - Mark Rubin, Dana-Farber Cancer Institute, Chair
  - Biospecimen Access and Ethical, Legal, and Policy Issues
    - Arthur Caplan, University of Pennsylvania, Chair
- Result: 1st Generation Guidelines for NCI biorepositories

Highlights of 1st Generation Guidelines

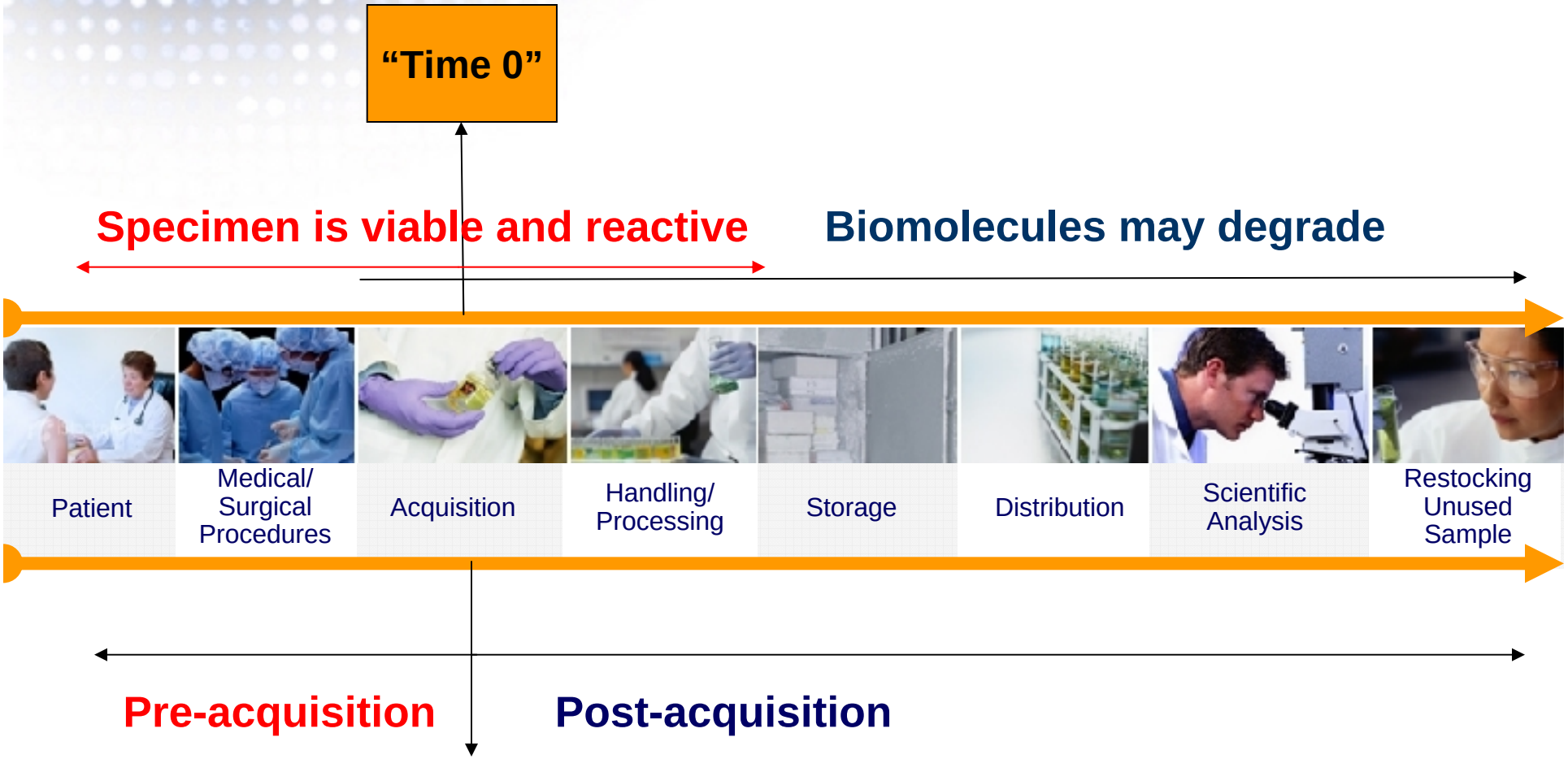
Recommendations for:

- Common best practices for research biorepositories
- Quality assurance and quality control programs
- Implementing enabling informatics systems
- Addressing ethical, legal, and policy issues
- Establishing reporting mechanisms
- Providing administration and management structure

NCI Office of Biorepositories and Biospecimen Research (OBBR)



Lifecycle of a Biospecimen: Biospecimen Research



Lifecycle of a Biospecimen: Biospecimen Research

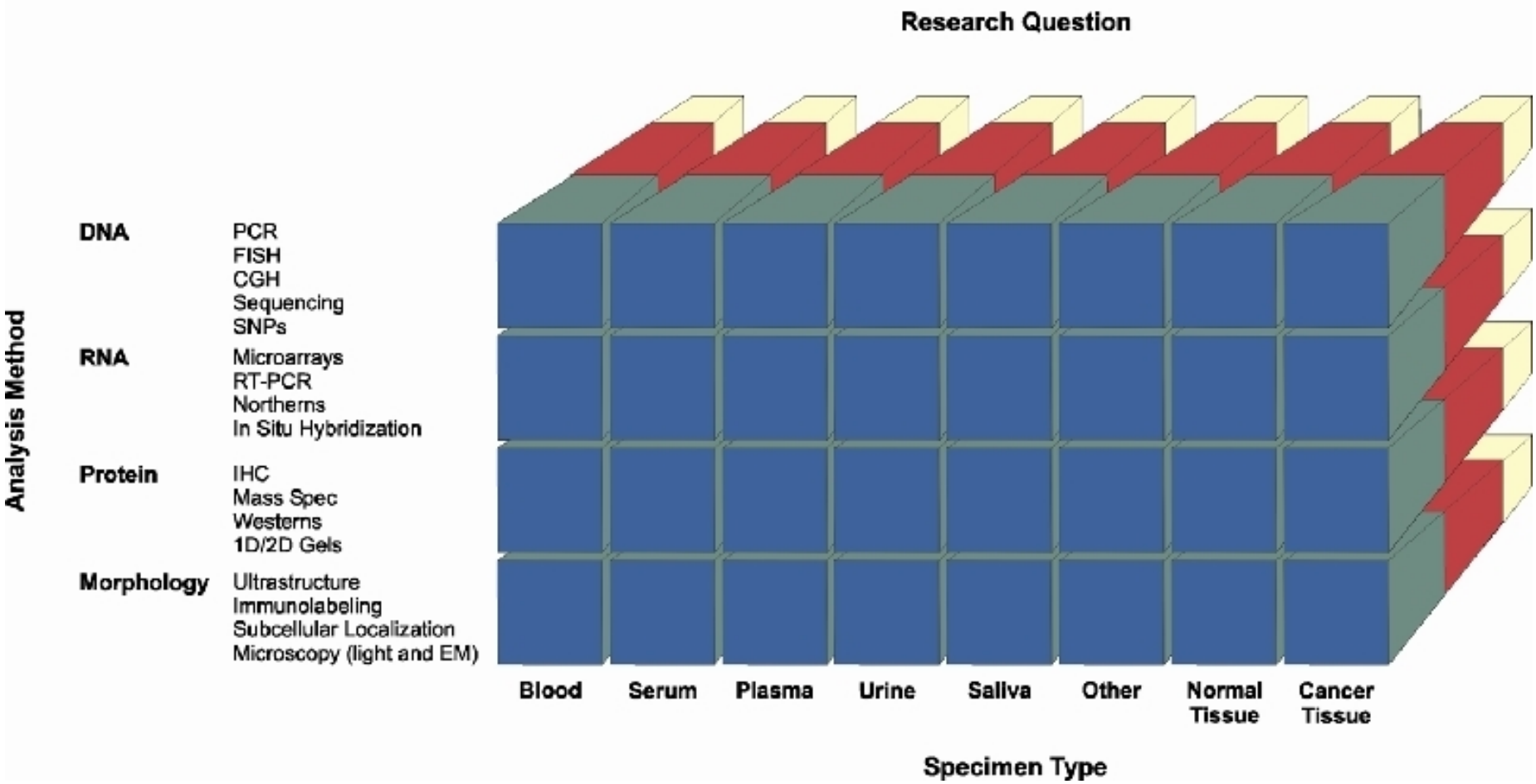
Post-acquisition variables:

- Time at room temperature
- Temperature of room
- Type of fixative
- Time in fixative
- Rate of freezing
- Size of aliquots
- Storage temperature
- Storage duration
- Storage in vacuum

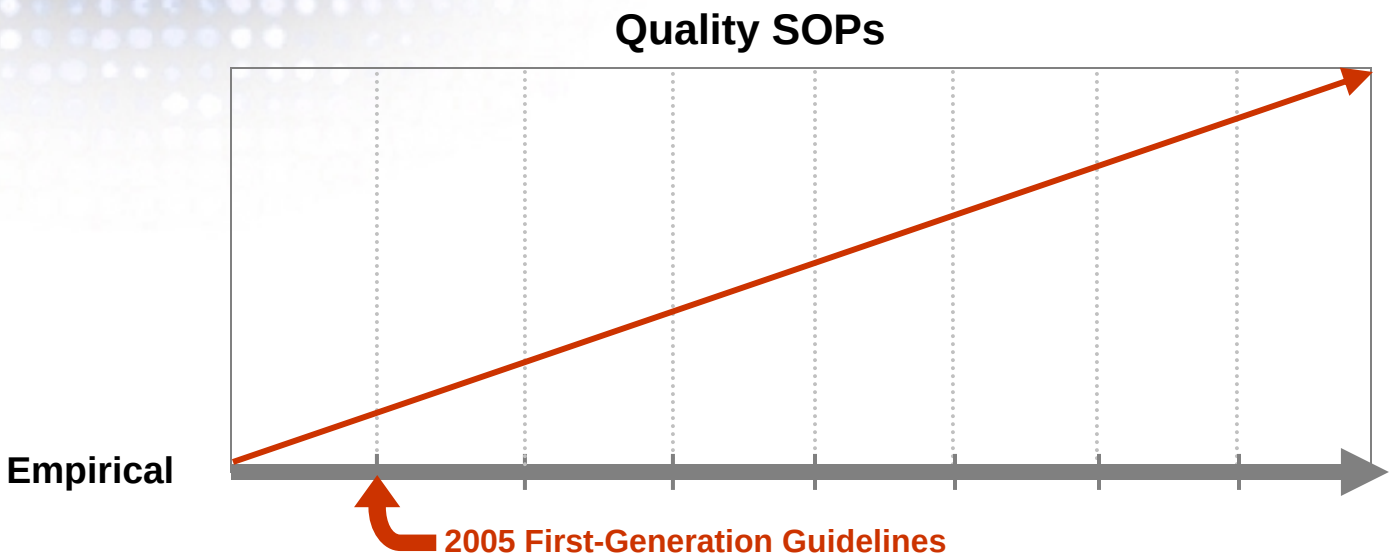
Pre-acquisition variables:

- Antibiotics
- Other drugs
- Type of anesthesia
- Duration of anesthesia
- Arterial clamp time
- Blood pressure variations
- Intra-op blood loss
- Intra-op blood administration
- Intra-op fluid administration

The "Ice-Cube Tray": Development of 2nd Generation Evidence-Based SOPs



Pathway to Scientifically Validated Biorepository Practices



Medical/ Surgical Procedures | Acquisition | Handling/ Processing | Storage | Distribution | QC/QA | Restocking Unused Sample

A New Paradigm

The Stone Age didn’t end because they ran out of stone.

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Charge to the Breakout Groups

Each breakout group will address the following issues:

- Which available, applicable prototype biospecimens should be chosen for initial BRN studies?
  - List 3 to 5 other types of biospecimens, if applicable, that might be prioritized for study.
- Which post-acquisition variables are most likely to affect the specific biomolecular profile in the biospecimen?
  - List in order of importance.

Charge to the Breakout Groups

- Which pre-acquisition variables are most likely to affect the specific bimolecular profile in the biospecimen?
  - List in order of importance.
- Which specific analytic platforms should the BRN focus on for assay of the biomolecules?
- Which investigators should be included in the BRN team to study the above questions?
- How should studies conducted in the BRN be quality controlled?

Filling in the Ice Cube Tray

- Priorities to be defined for BRN wet research:
  - Which biospecimens?
  - What variables?
  - What analysis platforms?
  - Which BRN investigators?
  - How to QC?
- Subtraction analysis from proposed dry research

Following this Retreat

- Retreat report issued to all participants
- Participants mini-profile to all participants
- Teams assembled
- Team meetings scheduled
- Protocols written
- Infrastructure and resource needs assessed
- IT linkages established
- Consent forms written, if applicable
- MTAs and contracts established
- Work begins by summer 2006

Breakout Groups: Session 1 (2 hours)

Group 1: Eiseman	Cancer tissue	DNA
Group 2: Shilling	Cancer tissue	RNA
Group 3: Jaffe	Cancer tissue	Protein / Morphology
Group 4: Cosentino	Serum/Plasma	Protein
Group 5: Hartge	Blood	DNA

Breakout Groups: Session 2 (2 hours)

Group 1: Juhl	Cancer tissue	DNA
Group 2: Bennett	Cancer tissue	RNA
Group 3: Calvo	Serum/Plasma	Protein
Group 4: Lemrow	Blood	DNA
Group 5: Camphausen	Urine	Protein

Launching a New Science

- Go to It!!!

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